

53. (Currently Amended~~New~~)

An oligonucleotide for preferentially killing cancerous cells over noncancerous cells comprising at least two CpG moieties and a nucleoside antimetabolite covalently linked to the oligonucleotide

The oligonucleotide of claim 51, wherein the antimetabolite is selected from the group consisting of 2'-deoxy-3'-thiacytidine, 3'-azido-3'-deoxythymidine, 2',3'-dideoxycytidine, 2',3'-didehydro-3'-deoxythymidine, 2',3'-dideoxyinosine, 5-fluoro-2'-deoxy uridine, 2-fluoro-9-b-D-arabinofuranosyladenine, 1-B-D-arabinofuranosylcytosine, 5-azacytidine, 5-aza-2'-deoxycytidine, 6-mercaptopurineriboside, 2-chlorodeoxyadenosine, pentostatin and a nucleoside antimetabolite for 2'-deoxy, 2',2'-difluorocytidine.

54. (Currently Amended~~New~~)

The oligonucleotide of claim 51 or 53, wherein two of said at least two CpG moieties are separated by a number of nucleotides selected from the numbers 2, 5, and 9.

55. (Currently Amended~~New~~)

The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is 5' to said at least two CpG moieties.

56. (Currently Amended~~New~~)

The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is 3' to said at least two CpG moieties.

57. (Currently Amended~~New~~)

The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is 3' to at least one CpG moiety and 5' to at least a second CpG moiety.

58. (Currently Amended~~New~~)

The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is linked to the oligonucleotide by a 3'-3' linkage.

59. (Currently Amended~~New~~)

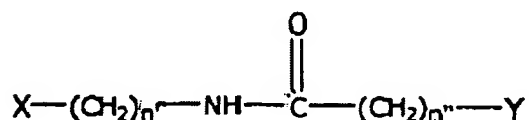
The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is linked to the oligonucleotide by a 5'-5' linkage.

60. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is linked to the oligonucleotide by a 3'-5' linkage.

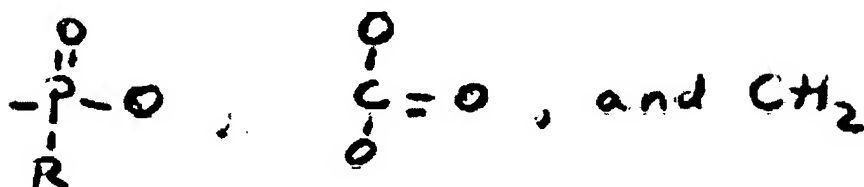
61. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is covalently linked to the oligonucleotide by a 5'-3' linkage.

62. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein said nucleoside antimetabolite is at a position that is selected from the following positions: 10 nucleotides upstream from one of the at least two CpG moieties, 9 nucleotides upstream from the CpG moiety, 8 nucleotides upstream from the CpG moiety, 7 nucleotides upstream from the CpG moiety, 6 nucleotides upstream from the CpG moiety, 5 nucleotides upstream from the CpG moiety, 4 nucleotides upstream from the CpG moiety, 3 nucleotides upstream from the CpG moiety, 2 nucleotides upstream from the CpG moiety, 1 nucleotides upstream from the CpG moiety, 10 nucleotides downstream from a CpG moiety, 9 nucleotides downstream from the CpG moiety, 8 nucleotides downstream from the CpG moiety, 7 nucleotides downstream from the CpG moiety, 6 nucleotides downstream from the CpG moiety, 5 nucleotides downstream from the CpG moiety, 4 nucleotides downstream from the CpG moiety, 3 nucleotides downstream from the CpG moiety, 2 nucleotides downstream from the CpG moiety, and 1 nucleotides downstream from the CpG moiety.

63. (Currently AmendedNew) The oligonucleotide of claim 51 or 53, wherein the nucleoside antimetabolite is covalently linked to the oligonucleotide by a linker having the formula.



wherein x and y are independently selected from



and R is selected from H, S, a C₁-C₆ alkyl, a C₁-C₆ alkoxy, and NH.

64. (Currently Amended~~New~~) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises at least one nucleotide having a ribose sugar moiety.

65. (Currently Amended~~New~~) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises at least one nucleotide having a 2'-deoxyribose sugar moiety.

66. (Currently Amended~~New~~) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises at least one 2'-halogen nucleotide.

67. (Currently Amended~~New~~) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises at least one 2'-N-alkyl nucleotide, wherein the alkyl has between about 1 and about 6 carbon atoms.

68. (Currently Amended~~New~~) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises at least one 2'-O-alkyl nucleotide, one 2'-N-Alkyl nucleotide, or one 2'-O-halogen nucleotide, wherein the alkyl has between about 1 and about 6 carbon atoms

69. (~~New~~Previously presented) The oligonucleotide of claim 68, wherein the alkyl is methyl.

70. (Currently Amended~~New~~) The oligonucleotide of claim 51 or 53, wherein the oligonucleotide comprises a plurality of nucleotides connected by covalent internucleoside linkages, wherein each of the linkages are selected from the group consisting of a phosphodiester

linkage, a C1-C6 alkoxy phosphotriester linkage, a phosphorothioate linkage and a phosphoramidate linkage.

71. (~~Currently Amended~~New) A pharmaceutical composition comprising the oligonucleotide of any of claims 51 or 53-70.

72. (~~Previously presented~~New) A pharmaceutical composition of claim 71 further comprising a pharmaceutically acceptable carrier.

73. (~~Previously presented~~New) The oligonucleotide of claim 72 wherein said pharmaceutically acceptable carrier is lipofectin.

74. (~~Previously presented~~New) An oligonucleotide for preferentially killing cancerous cells over noncancerous cells comprising a motif represented by one of the group of formulas 5'-PCGXCG-3' and 5'-CGXCGP-3', and wherein P is a nucleoside antimetabolite and X represents between 0 and 50 nucleotides.

75. (~~Currently Amended~~New)

An oligonucleotide for preferentially killing cancerous cells over noncancerous cells comprising a motif represented by one of the group of formulas 5'-PCGXCG-3' and 5'-CGXCGP-3', and wherein X represents between 0 and 50 nucleotides and P is a nucleoside

The oligonucleotide of claim 74, wherein the antimetabolite is selected from the group consisting of 2'-deoxy-3'-thiacytidine, 3'-azido-3'-deoxythymidine, 2',3'-dideoxycytidine, 2',3'-didehydro-3'-deoxythymidine, 2',3'-dideoxyinosine, 5-fluoro-2'-deoxy uridine, 2-fluoro-9-b-D-arabinofuranosyladenine, 1-B-D-arabinofuranosylcytosine, 5-azacytidine, 5-aza-2'-deoxycytidine, 6-mercaptapurineriboside, 2-chlorodeoxyadenosine, pentostatin and 2'-deoxy, 2' - ,2' -difluorocytidine.

76. (Currently Amended~~New~~) The oligonucleotide of claim of 74 or 75, where X is selected from the group consisting of 2, 5, and 9 nucleotides.

77. (Currently Amended~~New~~) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises multiple nucleotides and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 3'-3' linkage.

78. (Currently Amended~~New~~) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises multiple nucleotides and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 5'-5' linkage.

79. (Currently Amended~~New~~) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises multiple nucleotides and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 3'-5' linkage.

80. (Currently Amended~~New~~) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises 10 multiple nucleotides and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 5'-3' linkage.

81. (Currently Amended~~New~~) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises at least one nucleotide having a ribose sugar moiety.

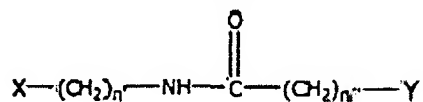
82. (Currently Amended~~New~~) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises at least one nucleotide having a 2'-deoxyribose sugar moiety.

83. (Currently Amended~~New~~) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises at

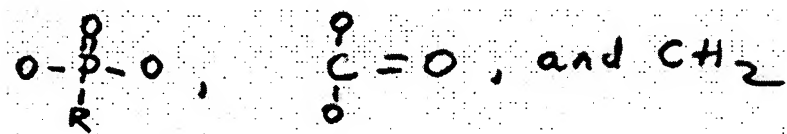
least one 2'-O-Alkyl nucleotide, 2'-N-Alkyl nucleotide, or 2'-O-halogen nucleotide, wherein the alkyl has between about 1 and about 6 carbon atoms.

84. (Currently Amended~~New~~) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises a plurality of nucleotides connected by covalent internucleoside linkages, wherein the linkages are selected from the group consisting of phosphodiester linkage, a C1-C6 alkoxy phosphotriester linkage, a phosphorothioate linkage and a phosphoramidate linkage.

85. (Currently Amended~~New~~) The oligonucleotide of claim 74 or 75, wherein the oligonucleotide comprises 30 multiple nucleotides and the nucleoside antimetabolite is attached to at least one of the multiple nucleotides by a linker having the formula.



wherein x and y are independently selected from



and R is selected from H, S, a C1-C6 alkyl, a C1-C6 alkoxy, and NH.

86. (Currently Amended~~New~~) A pharmaceutical composition comprising the oligonucleotide of any of claims 74-85.

87. (Currently Amended~~New~~) A pharmaceutical composition of claim 86 further comprising a pharmaceutically acceptable carrier.

88. (Currently Amended~~New~~) The oligonucleotide of claim 87 wherein said pharmaceutically acceptable carrier is lipofectin.

89. (~~Previously presented~~New) The method of synthesizing an oligonucleotide product for preferentially killing cancerous cells over non- cancerous cells comprising the steps of:

- (a) Selecting a oligonucleotide comprising at least two CpG moieties; and
- (b) Covalently linking a nucleoside antimetabolite to said oligonucleotide comprising at least two CpG moieties.

90. (~~Canceled~~New) ~~The method of claim 89, wherein said oligonucleotide comprising at least two CpG moieties comprises between 2 and 50 nucleotides.~~

91. (~~Currently Amended~~New)

The method of synthesizing an oligonucleotide product for preferentially killing cancerous cells over non- cancerous cells comprising the steps of:

- (a) Selecting a oligonucleotide comprising at least two CpG moieties; and
- (b) Covalently linking a nucleoside antimetabolite to said oligonucleotide comprising at least two CpG moieties,

The method of claim 89, wherein said nucleoside antimetabolite is - selected from the group consisting of 2'-deoxy-3'-thiacytidine, 3'-azido-3'-deoxythymidine, 2',3'-dideoxycytidine, 2',3'-didehydro-3'-deoxythymidine, 2',3'-dideoxyinosine, 5-fluoro-2'-deoxy uridine, 2-fluoro-9-b-D-arabinofuranosyladenine, 1-B-D-arabinofuranosylcytosine, 5-azacytidine, 5-aza-2'-deoxycytidine, 6-mercaptopurineriboside, 2-chlorodeoxyadenosine, pentostatin and antimetabolite for 2'-deoxy, 2',2'-difluorocytidine.

92. (New) The method of claim 89 or 91, wherein said oligonucleotide comprising at least two CpG moieties comprises between 2 and 50 nucleotides.